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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,579	03/22/2002	Lou Franciscus M. H. De Leij	Rijk-15(P52075US00	1723

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,579	DE LEIJ ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9 and 11-23* is/are pending in the application.

4a) Of the above claim(s) *11-13 and 15-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-9 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 4-9, 11-23 are pending in the application.

This Office Action is in response to the amendment filed on 2/1/06.

Response to Amendment

The rejection of claim 10 under 35 U.S.C. 101 is moot in light of Applicant's cancellation of the claim.

The rejection of claims 1-10 and 14 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment.

The rejection of claims 1-5, 7-10 under 35 U.S.C. 102 (b) has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 1, 2, 4-9 and 14 under 35 U.S.C.112 1st paragraph is maintained for reason set forth of the record mailed on 1/25/05 and further discussed below.

Election/Restrictions

Newly submitted claims 19-23 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 19-23 are drawn to a method of manufacture of a fusion construct, whereas the elected invention is an isolated nucleic acid. The nucleic acid of Group I is patentably distinct from the claimed method of claims 19-23 because the nucleic acid of Group I can also be made by chemical synthesis. As such, there would have been a search burden to examine these claims in a single application.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

on the merits. Accordingly, claims 11-13, 15-23 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Accordingly, claims 1, 2, 4-9 and 14 are currently under examination.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-9 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to this rejection, Applicants argue that the newly amended claim 1 reciting a nucleic acid having the sequence from –778 to –422 which includes mutant of said sequence that can be tested for their capacity to drive carcinoma-selective gene expression without undue experimentation. Applicants assert that promoter deletion studies, fusion contacts can be prepared of an equivalent sequence to be tested in epithelial and non-epithelial cell line to determine the extent of carcinoma-selectivity. Applicants thus conclude that the instant claims satisfy the written description requirement.

The above argument has been fully considered but deemed unpersuasive. The reasons for the written description rejection were discussed in detail in the office action mailed on 1/25/05.

In response to Applicant's argument, Applicant is reminded the guideline of written description as set forth in MPEP 2163R-2. It states: "The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." In the instant case, Applicants admit in the response filed on 2/1/06 (see page 6, 3rd paragraph) that the specification does not provide a description of the structural and functional definition of a functional equivalent of a nucleic acid sequence having the sequence from –778 to –422 of the sequence shown in Figure 1. According the guideline set forth in MPEP and cited above, description of an assay that makes or identifies the claimed invention alone does not constitute sufficient description of the claimed invention without structural and functional relationship. As discussed in the previous office action, the claims recite an isolated nucleic acid comprising a tissue specific promoter or functional equivalent thereof which directs selective gene expression in epithelium selective carcinoma cells. Such recitation potentially encompasses a large number of nucleic acid molecules of varying structure and sizes that have the function of direct epithelium carcinoma selective gene expression. However, the specification only teaches a 4.2 kb region at 5' of the GA733-2 gene and several fragments within this region that confers expression in SW948, an adenocarcinoma, and COS-7, but not in FLF (human fetal lung fibroblast) and HUVEC (human umbilical veins). The specification fails to teach whether these

fragments are lung carcinoma specific (as recited in claim 2). The specification also fails to teach regulatory regions of other genes of "functional equivalent" thereof that have claimed function of being carcinoma or lung carcinoma selective. Therefore, the specification fails to disclose a representative number of species by their complete structure nor their identifying characteristics. Thus, the written description requirement is not met, and this rejection is maintained.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this rejection, Applicants argue that the instant invention solves the problem of site of integration which affects that expression of the therapeutic gene. Applicants assert that the EGP-2 promoter driven gene will be position independent and expresses RNA as demonstrated in the transgenic mice studies presented in the instant specification, wherein the transgene expression is epithelium selective. Applicants further argue that the immunity argument is valid only if one introduces foreign cells comprising the therapeutic gene, wherein the gene therapy contemplated by the instant application relies upon the DNA based vectors, which the immune response argument is not relevant for the form of gene therapy with naked DNA as disclosed by Applicants. Applicants thus conclude that the amended claim 14 is enabled by the instant specification.

This argument has been fully considered but deemed unpersuasive. The detailed reason for the non-enablement of the claimed invention was set forth of the record mailed on 1/25/05.

In response to Applicant's argument of position independent expression of the EGP-2 promoter, Applicants are reminded that delivery of a therapeutic protein to a targeted site and achieving a therapeutic effect is different from expression of the human EGP-2 in a transgenic animal, wherein the latter only requires the integration of the transgene and expression of the gene product. In response to Applicant's argument that immune response is not relevant, Applicants are reminded that such effect is only one of the obstacles exists in the field of gene therapy. Furthermore, it is relevant to the current invention because the claims are not limiting the medicament with DNA based vector or therapeutic genes that would not elicit immune response. As such, for reasons discussed in the previous office action and above, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER